Estimating the transmissibility and severity of pandemic influenza

BJ Cowling

School of Public Health,
The University of Hong Kong, Hong Kong

September 8, 2010

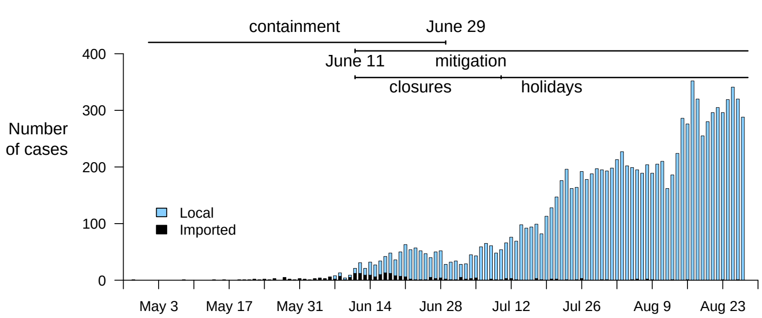
Acknowledgments

- Collaborators in Hong Kong: Joe Wu, Steven Riley, Gabriel Leung, Eric Lau, Malik Peiris
- Financial support:
  - The Research Fund for the Control of Infectious Disease, Food and Health Bureau, Government of the Hong Kong SAR (grant nos PHE-1, HK-09-04-01 and HK-09-04-04).
  - The Harvard Center for Communicable Disease Dynamics from the US NIH Models of Infectious Disease Agent Study program (grant no. 1 U54 GM088558).
  - The Area of Excellence Scheme of the Hong Kong University Grants Committee (grant no. AoE/M-12/06).

Background

- Estimating the transmissibility and severity of pandemic H1N1 was a priority in the early stages of the epidemic.
- Estimates of transmissibility may aid decisions about the potential impact of control measures, and also the effectiveness of those measures already implemented.
- Estimates of severity may aid decisions about ‘how hard’ to try to control transmission.
- But there are difficulties in obtaining these estimates . . .

First wave in Hong Kong



- Kindergarten and primary schools closed June 12 - early July.
- Summer holidays for all schools from early July onwards.
- 43 secondary schools closed after 1+ case confirmed.

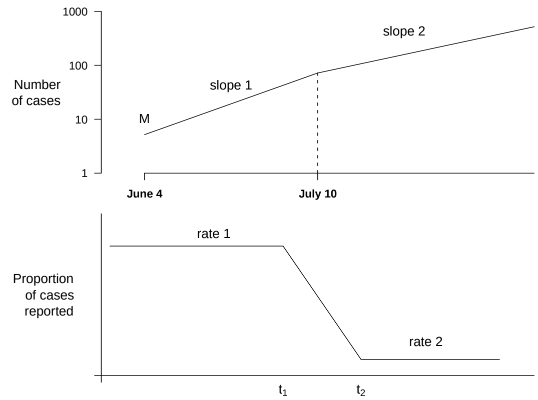
Changing case notification rate

- Laboratory-confirmed pandemic H1N1 was a notifiable disease throughout the first wave.
- Objective – to estimate the impact on influenza transmission of school closures and summer vacations.
- Problem – case identification rate likely changed during the switch from containment to mitigation phase

Modelling the impact of closures/vacations

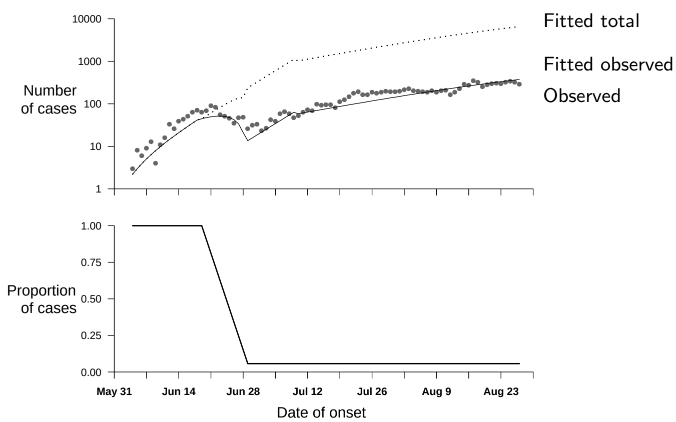
- JT Wu, BJ Cowling et al. Emerg Inf Dis 2010; 16:538-41.
- We used an age-structured S-I-R model to account for the non-linear transmission dynamics underlying the rising phase of the first wave of H1N1.
- We accounted in our model for the likely change in case identification rate as epidemic progressed and the public health response changed.
- We quantified transmissibility via the reproductive number R.

Model schematic

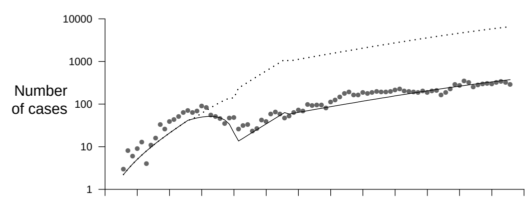


M, slope 1, slope 2, rate 1, rate 2, t_1 and t_2 estimated using MCMC.

Fitted model



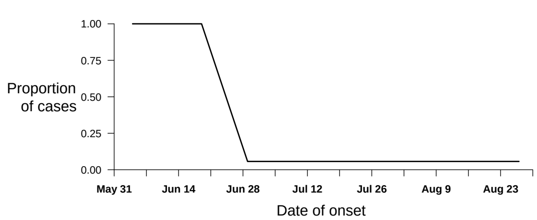
Fitted model



- $R \sim 1.7$ before June 11
- $R \sim 1.5$ between June 12 and July 10
- $R \sim 1.1$ after July 10
- Predicted illness attack rate of 2.5% (180,000 cases) by the end of August.

Fitted model

- We assumed 100% of cases were identified prior to mid-June.
- We estimated 5% of ill cases were identified in July-August.



Unknown proportion of population infected

- BJ Cowling, MSY Lau et al. Epidemiol 2010 (in press).
- Objective – to track dynamically H1N1 transmissibility through the first wave.
- Method – use Cauchemez' et al 2006 AJE method for real-time estimation of the daily effective reproductive number R_t (extension of Wallinga & Teunis 2004 AJE).
- Problem – reporting delays lead to biases in estimates in recent days . . .

Reporting delays

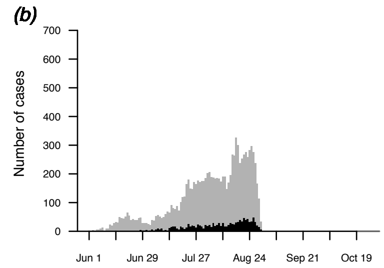


Figure: Reporting delays lead to an apparent drop-off in the epidemic over the most recent few days.

Methods – inferred infection networks

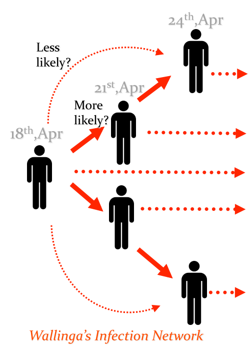


Figure: Wallinga and Teunis' infection network extended by Cauchemez to include cases not yet observed (i.e. to permit real-time analysis).

Empirical reporting delays

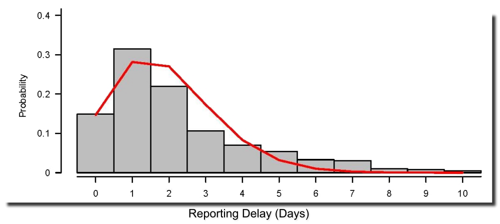


Figure: Reporting delays were well-represented by a Poisson distribution (red curve). For analysis of hospitalized confirmed cases a bivariate Poisson distribution was required for delays between onset, hospitalization and notification (not shown).

Real-time Rt in Hong Kong

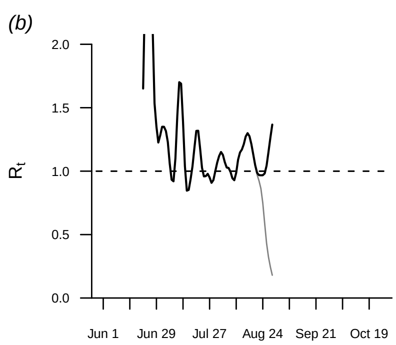
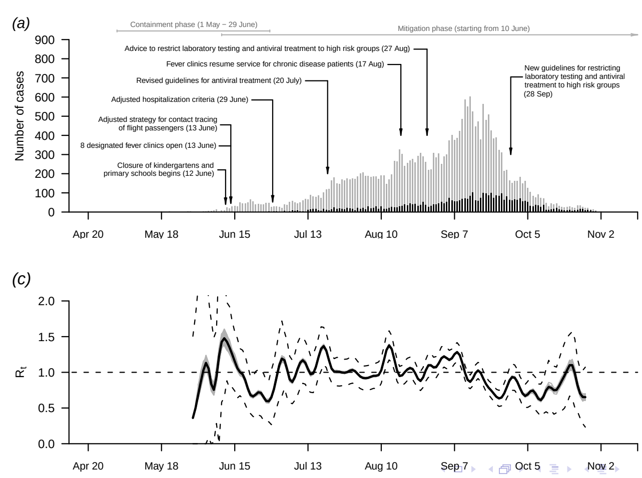
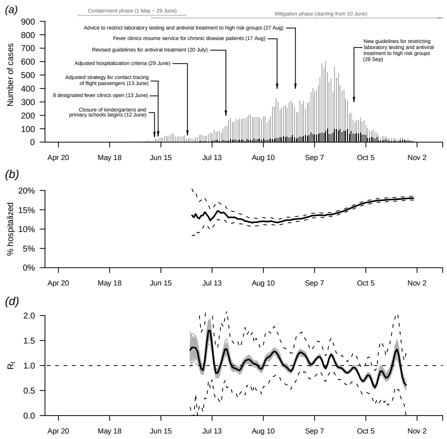


Figure: Real-time R_t by Cauchemez method (gray) and adjusting for reporting delays (black) using a data augmentation approach.

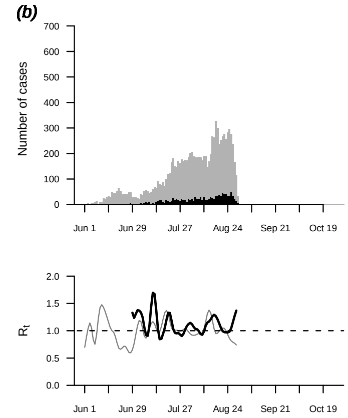
Rt based on notifications



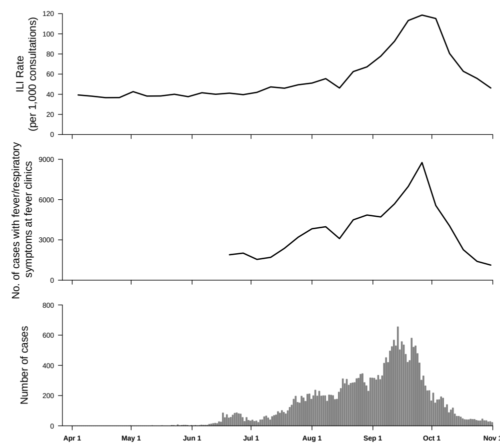
Rt based on hospitalizations



Real-time Rt similar for both time series



Routine surveillance data in Hong Kong



Unknown proportion of population infected

- Objective – to estimate the proportion of the population infected during the first wave.
- Problem – no clear denominators on routine outpatient surveillance.
- Solutions – conduct population-based surveillance on infections based on serology.

Serologic surveillance

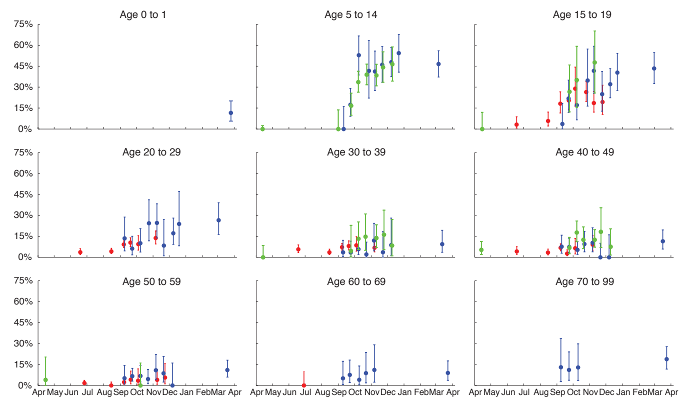
- JT Wu, BJ Cowling, JSM Peiris, Hong Kong Red Cross.
- Blood donors at 4 fixed centers across Hong Kong invited to provide sera for H1N1 antibody testing.
- $\sim$ 750 specimens collected every week since June 12, 2009.
- Serum specimens also collected from children participating in a community study, and medical and pediatric outpatients.

Serologic surveillance

- JT Wu, BJ Cowling, JSM Peiris, Hong Kong Red Cross.
- Blood donors at 4 fixed centers across Hong Kong invited to provide sera for H1N1 antibody testing.
- $\sim$ 750 specimens collected every week since June 12, 2009.
- Serum specimens also collected from children participating in a community study, and medical and pediatric outpatients.
- We can track the attack rate through time by studying the changes in prevalence of individuals with antibody titers $\geq 1:40$ (very low before first wave).
- Comparison with H1N1-associated admissions, deaths allows us to infer severity.

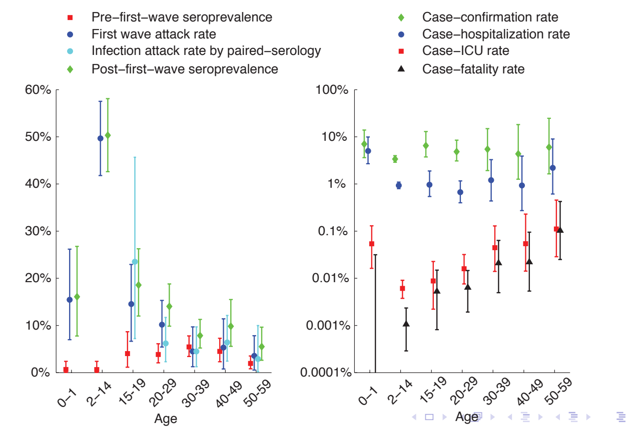
Agreement between three sources of data

Blood donors (n=7391), outpatients (n=3747) and community study (n=2161)



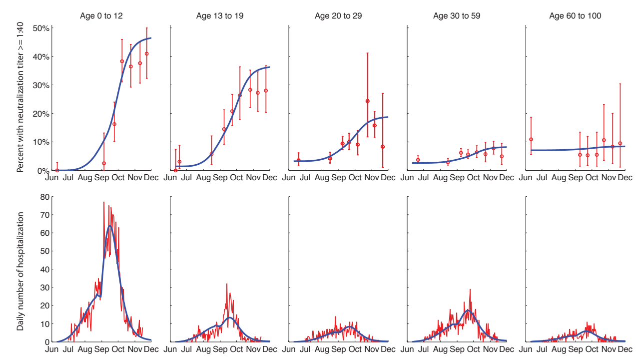
First wave attack rate and severity

Figure: Left: Estimated attack rate (blue). Right: Estimated severity.



Age-specific time course

Figure: Age-specific transmission model fitted to the proportion with viral neutralization titer $\geq 1:40$ (above) and hospitalizations (below).



Comments – impact of H1N1

- School closures and vacations were associated with substantial reductions in H1N1 transmissibility.
- Around 50% of school-age children infected in Hong Kong, but low attack rates in older adults.
- Severe illness much more common (per infection) with increasing age.

Implications for pandemic planning

- Routine laboratory testing of a defined subset of hospitalized cases for example all patients hospitalized with severe ARI in a subset of hospitals (Lipsitch et al. 2009 Lancet).
- Prospective cross-sectional serologic surveillance could allow timely information on transmissibility and severity, provided testing capacity exists.